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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/761,593 | 01/21/2004 | Lee-Hwei K. Sun | 02SUN2001-A | 3775 |

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| EXAMINER | |
|---|---|
| DEBERRY, REGINA M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/761,593 | SUN ET AL. | |
| | Examiner | Art Unit | |
| | Regina M. DeBerry | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *4,5,13 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,14 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/21/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-20, drawn to recombinant HuEPO-L-vFc fusion protein wherein human IgG2 has mutation SEQ ID NO:18, the CHO-derived cell line and method of making recombinant fusion protein, classified in class 435, subclass 69.1.

II. Claims 1-20, drawn to recombinant HuEPO-L-vFc fusion protein wherein human IgG4 has mutation SEQ ID NO:20, the CHO-derived cell line and method of making recombinant fusion protein, classified in class 435, subclass 69.1.

III. Claims 1-20, drawn to recombinant HuEPO-L-vFc fusion protein wherein human IgG1 has mutation SEQ ID NO:22, the CHO-derived cell line and method of making recombinant fusion protein, classified in class 435, subclass 69.1.

The inventions are distinct, each from the other because of the following reasons:

**Inventions I-III are unrelated products.** Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Groups I-III are directed to products (HuEPO-L-vFc fusion protein) that are

distinct both physically and functionally, are not required one for the other, and are therefore patentably distinct. Groups I-III have structures being made up of completely different building blocks. Amino acid sequences of different polypeptides are structurally distinct chemical compounds and are unrelated to one another. These very diverse structures result in completely different modes of operation and modes of function and effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, separate search requirements, and/or recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Hsiang-ning Sun on 18 May 2006, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-3, 6-15, 20 (which read upon SEQ ID NO:18). Affirmation of this election must be made by applicant in replying to this Office action. Claims 4, 5, 16-19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claim 13 will also withdrawn because it reads on SEQ ID NO:20 (G4 variant).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-3, 6-12, 14, 15 and 20 are under examination.

### *Information Disclosure Statement*

The information disclosure statement(s)(IDS) filed 10 December 2004 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

### *Claim Objections*

Claims 9 and 20 are objected to because of the following informalities: The instant claims encompass a non-elected invention and require amendment to limit to elected invention.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, 6-12, 14 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 9, 11 and 20 are indefinite because of the recitation, "..**about** 20 or fewer amino acids..". It is unclear if "..**about** 20 or fewer amino acids" means 30, 25 or 19 amino acids. The metes and bounds of the instant claims cannot be determined.

Claims 2, 3 and 6 are indefinite because it lacks antecedent basis. Amending the instant claims to recite, "The recombinant HuEPO-L-vFc fusion protein of claim 1, wherein the peptide linker.." (claim 2), The recombinant HuEPO-L-vFc fusion protein of claims 1 or 2, wherein the human IgG Fc variant.." (claim 3) and "The recombinant HuEPO-L-vFc fusion protein of any.." (claim 6) would be remedial.

Claims 7-10 and 20 are rejected because the term "CHO-derived cell line" is unclear. It is suggested that the instant claims be amended to recite, "..CHO cell line transfected with DNA encoding the recombinant HuEPO-L-vFC fusion protein..."

Claims 3, 9, 14 and 20 are indefinite because of the recitation, "..**as** SEQ ID NO:18..". Amending the claims to recite, "**of** SEQ ID NO:18" would be remedial.

Claim 12 is indefinite because it is missing the SEQ ID NO:. The metes and bounds of the instant claim cannot be determined.

Claim 14 is indefinite because of the recitation, "human IgG1 with Leu234Val, Leu235Ala, and Pro331Ser mutations as SEQ ID NO:18. The instant specification teaches this sequence as SEQ ID NO:22 a G1 variant (see instant specification, paragraph 0014 and Figure 1). The metes and bounds of the instant claim cannot be determined.

Claim 10 is indefinite. It is suggested that the instant claim be amended to recite, "..**wherein said** method comprises:." (2nd line). It is suggested that the instant

claim be amended to recite, "..under conditions, **wherein the recombinant fusion protein**.." (3rd-4th line). It is suggested that the instant claim be amended to recite, "..purifying the expressed **recombinant fusion protein**.." (5th line).

Claim 20 is indefinite. It is suggested that the instant claim be amended to recite, "..**wherein said** method comprises:." (2nd line). It is suggested that the instant claim be amended to recite, "..under conditions, **wherein the recombinant fusion protein**.." (3rd-4th line). It is suggested that the instant claim be amended to recite, "..purifying the expressed **recombinant fusion protein**.." (5th line).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 6-8, 10, 11 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a recombinant HuEPO-L-vFc fusion protein, consisting of HuEPO, a peptide linker and a human IgG Fc variant, wherein the human IgG Fc variant comprises a hinge, CH2, and CH3 domains of human IgG2 with Pro331Ser mutation as SEQ ID NO:18,

does not reasonably provide enablement for:

a recombinant HuEPO-L-vFc fusion protein, **comprising** HuEPO, a peptide linker and a **human IgG Fc variant.**

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant specification teaches the cloning of HuEPO-L-vFc fusion proteins. The fusion protein contains an IgG Fc variant, which consist of a hinge, a CH2 and a CH3 domain wherein detailed amino acid mutations are made within the CH2 domain. The instant claims, however, read on *any human IgG Fc variant* which allows for the IgG Fc variants to comprise various mutations. In addition, the instant claims recite, "..HuEPO-L-vFc fusion protein, **comprising**..", which allows for the HuEPO-L-vFc fusion proteins to comprise other sequences, mutations and/or variants. *The instant working examples teach a biological function with a specific fusion protein comprising specific IgG Fc variants.* While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517). Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the structure and still maintain

sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 3 is rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. US 6,900,292 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 3 of the instant application recites, "the human IgG Fc variant in claim 1 or claim 2 comprising a hinge, CH2 and CH3 domains of human IgG2 with Pro331Ser mutation as SEQ ID NO:18". Instant claim 3 depends from claim 1, which is drawn to a recombinant HuEPO-L-vFC fusion protein comprising HuEPO, a peptide linker, and a human IgG Fc variant. Claim 1 of U.S. Patent No. US 6,900,292 B2 is drawn to a recombinant HuEPO-L-vFC fusion protein consisting of HuEPO, a peptide linker, and a human IgG Fc variant, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 with Pro331Ser mutation as SEQ ID NO:18. Both claims are drawn to a fusion HuEPO-L-vFc fusion protein wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 with Pro331Ser mutation as SEQ ID NO:18.

It is noted that the claims of U.S. Patent No. US 6,900,292 B2 recite IgG Fc variants of SEQ ID NO:18. Applicant is warned that the instant claims, depending on how they are amended, could later be rejected under a statutory type (35 U.S.C. 101) double patenting rejection. Only canceling or amending the conflicting claims so they are no longer coextensive in scope can overcome this type of rejection. The filing of a

terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
5/11/06

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER

5/24/06

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